REMARKS

Claim amendments and cancellation of claim 8 are hereby introduced not to narrow the scope of the pending claims, but to recite subject matter that is comprised within elected Group I as set forth in the Office Action dated October 23, 2002, and subsequent election by Applicants. These amendments and claim cancellation are made without prejudice, and Applicants reserve the right to assert claims by appropriate continuation and/or divisional practice to subject matter that is removed from the present claims.

Claim amendments to correct typographical errors in claims 39 and 41 and in the written description at pages 117 and 123 are hereby introduced. These amendments simply change notation.

A copy of the IDS mailed September 27, 2002, (Third Supplemental IDS) is attached hereto. This Attachment "A" comprises copies of the filing and transmittal materials for such IDS, Information Disclosure Statement, PTO-1449A, and Submission Under MPEP 609D. It is believed that this is the IDS of which the Examiner requests a copy. *See* Office Action, item 8. Should the Examiner refer in the Office Action to some other filing, Applicants respectfully request that they be notified accordingly, so that copies can be provided.

Applicants do hereby bring to the attention of the Examiner that there are presently two pending related cases that are U.S. Serial Numbers 09/947,041, filed on September 5, 2001, and 10/075,673, filed on February 13, 2002. Copies of Office Actions issued in such two cases are attached hereto as Attachment "B".

Claims 46-47 are cancelled. This claim cancellation does not imply the withdrawal of claimed subject matter. Instead, these claims are cancelled herein because corresponding claims have been introduced in the pending applications 09/947,041 and 10/075,673 referred to above.

The related-application data introduced by this amendment are not the addition of new benefit claims, but simply claims that had been asserted elsewhere in the filing materials. For example, priority claims are asserted in the oath/declaration submitted with the filing materials.

The Office Action Summary lists claim 8 as being allowed. However, the Detailed Action, p. 2, indicates that claim 8 stands withdrawn. In light of the elected group of claims and the subject matter recited in claim 8, Applicants believe that the disposal of claim 8 as allowed on the Office Action Summary is due to a typographical error. Should this understanding by Applicants be incorrect, it is respectfully requested that Applicants be advised appropriately in the next communication from the Examiner.

Applicants believe that the present claim amendments in connection with the elected subject matter address the Markush Rejection asserted in the Office Action and therefore request that such rejection be withdrawn.

The Office Action refers to the following references: "X" references cited in the corresponding PCT Search Report, and articles cited on Form PTO-982. To facilitate the discussion below, these references are identified as follows:

(1) S. Andronati, *et al.*, "Synthesis of ... indazole derivatives and their affinity to 5-HT1a serotonin and dopamine D1 receptors", Pharmazie **54(2)**, 99-101 (1999) (hereinafter "Andronati");

(2) Yasuo Fujimura, *et al.*, "Indazole derivatives", JP 52 014765 A (Chugai Pharmaceutical Co., Ltd., Japan) (hereinafter "Fujimura1");

(3) Yasuo Fujimura, *et al.*, "Indazole derivatives", JP 50 116470 A (Chugai Pharmaceutical Co., Ltd., Japan) (hereinafter "Fujimura2");

(4) GB 1 489 280 A (Chugai Pharmaceutical Co., Ltd.) (hereinafter the "British Patent");

(5) U.S. 5,599,815 "Antipsychotic benzoisothiazolyl piperazine derivatives" (hereinafter the "'815 patent"). As per the patent information provided in the search report attached to the Office Action, this is the US equivalent to reference "U" in Form PTO-982 cited in the Office Action.

(6) Reference "X" listed in Form PTO-982 cited in the Office Action is precisely Andronati, already cited in the PCT Search Report. See item (1) above.

(7) Reference "W" listed in Form PTO-982 cited in the Office Action corresponds, as per patent information provided in the search report attached to the Office Action, with US 6,020,336 and US 6,046,205,

"Indole and indazole compounds" (hereinafter the "'336 and '205 patents").

(8) M.H. Paluchowska, *et al.*, "Influence of the aliphatic spacer length on the 5-HT1A receptor activity of new arylpiperazines with an indazole system", Polish J. Pharmacology **52(3)**, 209-216 (2000) (hereinafter "Paluchowska1").

(9) M.H. Paluchowska, *et al.*, "Structure-activity relationship studies of CNS agents. 40. Effect of the amide fragment on 5-HT1A receptor activity of some analogs of MP 3022", Polish J. Pharmacology **51(5)**, 415-421 (1999) (hereinafter "Paluchowska2").

Items (1)-(4) are the "X" references listed in the International Search Report PCT/US 01/25289. Items (5)-(9) are the references cited in Form PTO-982 that was attached to the Office Action. Copies of these items are attached hereto in Attachment "C". Documents that are not in English in their original form are provided in their original forms and also as English translations. The reasoning below is set forth as being applicable to any one and all the relevant portions of the references that the search report provided with the Office Action classifies as being equivalent items or counterparts.

As reasoned below, Applicants respectfully submit that these references do not support rejections under 35 U.S.C. §§ 102, 103, against the claimed subject matter and equivalents thereof, and respectfully request that such rejections be withdrawn.

Andronati (items (1) and (6)) discloses indazole derivatives and reports on "the affinity of 3-aryl-[(4-phenyl-1-piperazinyl)butyl]indazole derivatives to both 5-HT_{1A} serotonin and D_1 dopamine receptors and to reveal the perspective biologically active compounds of this series." Andronati, p. 99, col. 2. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed in Andronati and the subject matter claimed in the pending claims. Even if the

differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that Andronati does not disclose the claimed subject matter and thus Andronati may not anticipate the pending claims.

Fujimura1 (item (2)) discloses "a method for manufacturing an indazole derivative having the general formula" given therein at p. 1, col. 2. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed in Fujimura1 and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that Fujimura1 does not disclose the claimed subject matter and thus Fujimura1 may not anticipate the pending claims.

Fujimura2 (item (3)) discloses a method for manufacturing an indazole derivative having general formula (I) given therein at p. 1, col. 2. Because of the disclosure in Fujimura2, the reasoning set forth regarding Fujimura1 applies to Fujimura2; such reasoning is incorporated with respect to Fujimura2, which for at least the reasons set forth in regard to Fujimura1 does not disclose the claimed subject matter and thus Fujimura2 may not anticipate the pending claims.

The British Patent (item (4)) discloses indazole derivatives having formula (I) given therein at p. 1, between lines 5 and 10. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed

in Fujimura1 and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that the British Patent does not disclose the claimed subject matter and thus the British Patent may not anticipate the pending claims.

The '815 patent (item (5)) discloses benzoisothiazolyl piperazine derivatives, some of which comprising an indazole moiety derivative. *See* the '815 patent, general formula (I) and structure (iv), col. 2, *ll.* 3-9, 25-33. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed in the '815 patent and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that the '815 patent does not disclose the claimed subject matter and thus the '815 patent may not anticipate the pending claims.

The '336 and '205 patents (item (7)) disclose indole and indazole compounds. *See* the '336 and '205 patents, formula (I), col. 2. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed in the '336 and the '205 patents and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these

differences show that the '336 and the '205 patents do not disclose the claimed subject matter and thus the '336 and the '205 patent may not anticipate the pending claims.

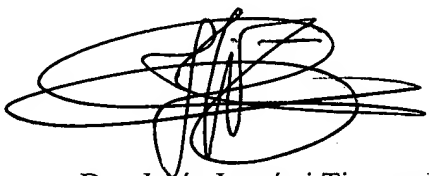
Paluchowska1 (item (8)) discloses arylpiperazine derivatives that contain a terminal 1- or 2-indazolyl fragment and a methylene spacer of various carbon-member lengths. *See, e.g.,* Paluchowska1, Abstract, general structure and table given in Fig. 1, therein. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7- membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed in Paluchowska1 and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that Paluchowska1 does not disclose the claimed subject matter and thus Paluchowska1 may not anticipate the pending claims.

Paluchowska2 (item (9)) discloses arylpiperazine derivatives that contain a terminal 1- or 2-indazolyl, 1- or 2-benzotriazolyl, or phenyl fragment and a methylene spacer of various carbon-member lengths, optionally with an amide bond in such spacer. *See, e.g.,* Paluchowska2, Abstract, general structure and table given in Fig. 1, therein. In contrast, the pending claims recite, *inter alia*, compounds that comprise an entity with "R^5 and R^6 ... taken together to form pyridinyl or a 5-membered carbocyclic ring or 7-membered carbocyclic ring, which ring may be unsaturated or aromatic, and each of said pyridinyl, 5-membered ring and 7-membered ring may be optionally substituted with ...". Claim 1. Dependent claims recite, *inter alia*, compounds that are consistent with this generic recitation in claim 1. There are further differences and distinguishing features between the structures disclosed in Paluchowska2 and the subject matter claimed in the pending claims. Even if the differences based on the explicitly quoted structural feature recitations were the only differences between the reference disclosure and the recited subject matter, these differences show that Paluchowska2 does not disclose the claimed subject matter and thus Paluchowska2 may not anticipate the pending claims.

The differences indicated above show that the references do not teach or suggest all the claim limitations. In addition, it has not been established that there is any suggestion or motivation to modify any of the references to generate the claimed subject matter. Furthermore, it has not been established that, absent the teachings provided by Applicants, there is any reasonable expectation of success regarding the claimed subject matter. Because none of the references discloses any activity or modulating capability with respect to cathepsin S, none of such references provides any suggestion or motivation to modify the structures disclosed in the references to arrive at the presently claimed compounds, and none of such references leads to an expectation of success of the compounds claimed in the present claims. Because of at least these reasons, the cited references may not render the pending claims obvious.

Applicants respectfully request favorable consideration of the present Amendment and Response to place the present application in condition for allowance.

Respectfully submitted,



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Dated: May 28, 2004